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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/527,919	03/17/00	CHATFIELD S	KC01002US

EXAMINER	
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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trad marks

Office Action Summary	Application N .	Applicant(s)	
	09/527,919	CHATFIELD, STEVEN NEVILLE	
	Examiner	Art Unit	
	Bao Qun Li	1648	

-- The MAILING DATE of this communication appears n the cover sheet with the correspondence address --

Peri d for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 October 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-34* is/are pending in the application.

4a) Of the above claim(s) *5-9,11-17 and 19-34* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,10 and 18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *8* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claims 1-34 are pending

Election/Restrictions

Applicant's election with traverse of Group I, claims 1-4, 10 and 15 within the scope of a full length of tetanus toxin fragment C fused with 20 amino acid of pre-S1 region of HBV peptide in Paper No. 13 is acknowledged. The traversal is on the ground(s) that searching the entire application cannot be a serious burden.

Since the claimed inventions are drawn to structurally and functionally different fusion peptides, and each of them constitutes a patenable distinctive invention, examiner partially agrees with the applicants' argument and agrees to rejoin the polypeptide or immunological composition compromising the polypeptide encoded by S1 HBV fused with a full length of tetanus toxin fragment C. In this regard, claims 11 and 18 are rejoined with the elected group I.

During the reconsideration of the restricted group, examiner also found that claim 15, which is directed to a polynucleotide, is improperly restricted into the group I. Therefore, the claim 15 is withdrawn from group I and regrouped into group II.

In summary, claims 1-4, 10 and 18 in the scope of a full length of tetanus toxin fragment C fused with the peptide encoded by pre-S1 region of HBV are considered by the examiner.

Applicants are required to amend the claims 1-4, 10 and 18 within the scope of a full length of tetanus toxin fused with peptide encoded by S1 region to reflect the examination on the merits. Applicants are also reminded to cancel the claims 5-9, 11-17, 19-34 to the non-elected group.

Claim Objections

Claim 4 is objected to because of the following informalities: a "," is missing after the pre-S1 region of at least 20 amino acids on the second line of the claim. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-4 10 and 18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-3 are vague and indefinite in that the metes and bonds of the recited "region" of fragment thereof are not defined. The claims are interpreted in light of the specification, however, the specification fails to teach what are the definitions for the "region" or "fragment thereof"? The claims should point out precisely which sequence structure of the "region" of fragment thereof' of HBV pre-S1 is intended. This affects the dependent claims 4, 10 and 18.

In addition, the claims 1 and 4 are also unclear for recitation that peptide comprising at least 6 or 20 amino acids. Since there is no given upper limitation of the envelope components in the said claims, is 50 amino acids intended? Therefore, the claims are considered as indefinite. This also affects the dependent claims 2-3, 10 and 18.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 10 and 18 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for constructing fusion peptide consisting of at least 6 amino acids sequence of pre-S1 HBV peptide fused with the full length of the tetanus toxin fragment C, does not reasonably provide enablement for having a vaccine made from HBV pre-S1 peptide in any length fused tetanus toxin fragment C in any length. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The test of scope of the enablement is whether one skilled in the art could make and use the claimed invention from the disclosure in the application coupled with information known in the art would undue experimentation (See United States v. Theketronic Inc., 8USPQ2d 1217 (fed Cir. 1988). Whether undue experimentation is required is not based upon a single factor but rather a conclusion reached by weighting many factors. Theses factors were outlined in Ex parte

Forman, 230 USPQ 546 (Bd. Pat. App. & Inter. 1986) and gain in re Wands, 8USPQ2d 1400 (Fed. Cir. 1988).

The recombinant HBV vaccines comprising either single HBV S antigen or a triple antigen (S, pre-S1 and pre-S2) have been used for as vaccines for almost 2 decades. However, a recent comparative study of a triple antigen and a single antigen recombinant vaccine for adult has demonstrated that the single antigen of HBV vaccine produce less protective immunity (83%) than the triple antigen vaccine of HBV (97%) as evidenced by Young et al (J. Med. Virol. 2001, Vol. 64, pp. 290-298, see abstract), indicating the unpredictability of using single HBV pre-S1 or its fragment along as a vaccine antigen.

In the instate case, Applicant presents that fusion protein comprising pre-S1or pre-S1/pre-S2 fused to full length tetanus toxin C fragment can induce an pre-S1 antibody in mice. However, there are no working example for whether the said antibody can be raised in human body and produce a protective immunity against the HBV infection.

Applicants also present no guidance on how the skilled artisan would practice successfully a vaccine comprising the claimed fusion peptide. Since the scope of the claims read on vaccine, a suitable animal model that shows the claimed pre-S1 fusion peptide can protect animal from a HBV challenge is required. An antibody production from a mice injected with a different antigen constructs cannot represent an antibody production against another antigen construct even the two antigen constructs share certain homology. More importantly, there is no indication that the antibody produced by a pre-S1 antigen consisting of at least 6 amino acids fused with tetanus toxin C fragment can produce a protective immunity against HBV infection.

Therefore, considering large quantity of experimentation needed, the unpredictability of the field, the state of the art, and breadth of the claims, it is concluded that undue experimentation would be required to enable the intended claim.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1-4, 10, and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mimms et al. (EP-A-0 389 983), Khan et al. (WO 94/03615) and Shi et al. (Vaccine 1995, Vol. 13, pp. 933-937).

The present invention relates to a fusion protein derived from hepatitis B (HBV) surface protein epitope pre-S1 fused with C fragment of tetanus toxin (tetC). TetC is higly immunogenic and appears to be used therein as a carrier protein to improve the immune response of the animal or human body to HBV infection. The fusion protein is linked by a hinge region to make sure that the proteins fold correctly. The application also related to the vaccine comprising the same.

The fusion protein of tetC and its fragment that can be used as a carrier protein with different antigen determinants have been wildly described before as evidenced by Khan et al. He explicitly suggests that tetC can be fused with HBV for inducing a protective immunity against HBV (page 5, line 10 through page 6, line 4). Khan et al. differ from the claimed polypeptide in that they do not specifically identify the suitable HBV epitopes that are used for the suggested application.

However, the epitopes of HBV pre-s protein are well documented in the prior arts, For example, Mimms et al. discloses several immunogenic epitopes for producing anti-pre-S1 and pre-S2 antibodies as well as the therapeutic application of the antibodies (see example 4). Mimms et al. differ from the claimed polypeptide in that they do not use the antigen comprising tetC fused with HBV pre-S1 or pre-S2 peptide.

Shi et al. teach to use a cholera toxin B (CTB) subunit as a carrier protein to fuse with HBV pre-S2 antigen to stimulate the immune response (see page 933, left-hand column, last paragraph). The function of the CTB used here exhibits the same function as disclosed by Khan et al.

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention was filled to be motivated by the recited references and to combine the method taught

by Khan et al. and Mimms et al. in further view of the teaching from Shi et al. to make a fusion peptide or a immunogenic composition comprising the well characterized HBV pre-S1 epitope fused with tetC as disclosed by Khan et al. to administering into a host animal to see the immune response without unexpected results. Hence the claimed invention as a whole is prima facie obvious absence unexpected results.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bao Qun Li whose telephone number is 703-305-1695. The examiner can normally be reached on 8:00 to 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 703-308-4027. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Bao Qun Li

Baoqun Li

October 16, 2001

ALI R. SALIMI
PRIMARY EXAMINER